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ORIGINAL ARTICLES
Economic Evaluation

High-Dose Hemodialysis versus Conventional In-Center Hemodialysis: A Cost-Utility Analysis from a UK Payer Perspective

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ABSTRACT

Objective: To investigate the cost-effectiveness of high-dose hemodialysis (HD) versus conventional in-center HD (ICHD), over a lifetime time horizon from the UK payer's perspective. **Methods:** We used a Markov modeling approach to compare high-dose HD (in-center or at home) with conventional ICHD using current and hypothetical home HD reimbursement tariffs in England. Sensitivity analyses tested the robustness of the results. The main outcome measure was the incremental cost-effectiveness ratio (ICER) expressed as a cost per quality-adjusted life-year (QALY). **Results:** Over a lifetime, high-dose HD in-center (5 sessions/wk) is associated with higher per-patient costs and QALYs (increases of £108,713 and 0.862, respectively) versus conventional ICHD. The corresponding ICER (£126,106/QALY) indicates that high-dose HD in-center is not cost-effective versus conventional ICHD at a UK willingness-to-pay threshold of £20,000 to £30,000. High-dose HD at home is associated with lower total costs (£522 less per patient) and a per-patient QALY increase of 1.273 compared with ICHD under the current Payment-by Results reimbursement tariff (£456/wk). At an increased home HD tariff (£575/wk), the ICER for high-dose HD at home versus conventional ICHD is £17,404/QALY. High-dose HD at home had a 62% to 84% probability of being cost-effective at a willingness-to-pay threshold of £20,000 to £30,000/QALY. **Conclusions:** Although high-dose HD has the potential to offer improved clinical and quality-of-life outcomes over conventional ICHD, under the current UK Payment-by Results reimbursement scheme, it would be considered cost-effective from a UK payer perspective only if conducted at home.

Keywords: cost-effectiveness analysis, cost-utility analysis, end-stage renal disease, high-dose hemodialysis, in-center hemodialysis.

Introduction

End-stage renal disease (ESRD) is an irreversible decline in kidney function that, without dialysis or kidney transplantation (renal replacement therapy [RRT]), is fatal. In the United Kingdom and globally, ESRD poses a substantial health and economic burden. In 2009-2010, the England National Health Service (NHS) spent an estimated £1.45 billion (~1.3% of all NHS spending) on chronic kidney disease. Half this amount was spent providing RRT to patients with ESRD even though patients receiving RRT represent only 2% of the population with chronic kidney disease [1].

The two main dialysis modalities are hemodialysis (HD) and peritoneal dialysis (PD). HD is generally performed in a hospital or satellite unit but can be performed at home in suitable patients (home hemodialysis [home HD]). In the United Kingdom, 80% of prevalent dialysis patients receive conventional HD, usually 3 sessions/wk and 3 to 5 hours a session [2]. Evidence suggests, however, that clinical and quality-of-life (QOL) outcomes can be improved with higher doses of HD by increasing the frequency and/or duration of treatment via short-daily, quotidian or nocturnal HD. Three randomized controlled trials reported that frequent nocturnal HD and six times weekly in-center HD (ICHD) were

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associated with clinically significant improvements in selected clinical and QOL measures versus conventional, thrice-weekly HD [3–5]. Several observational and retrospective studies reported 36% to 61% reductions in mortality in patients receiving high-dose HD versus conventional HD [6–8]. Home HD has further benefits: patients have greater control over their dialysis schedule, fewer travel requirements, and are less exposed to hospital pathogens [9].

Previously published cost-effectiveness analyses of high-dose HD versus conventional ICHD are based on earlier evidence. Recent clinical and humanistic evidence warrants a reevaluation of the cost-effectiveness of high-dose HD. Although an earlier NHS analysis showed that home HD was associated with lower costs and better outcomes than was ICHD, increased dialysis frequency, duration, or both were not included in its main evaluation [10]. A 2003 National Institute for Health and Care Excellence (NICE) appraisal of home HD considered the cost-effectiveness of short-daily and nocturnal home HD, but only in sensitivity analysis [9]. The current analysis assesses the cost-effectiveness of high-dose HD (in-center or at home) versus conventional ICHD over a lifetime time horizon from a UK payer perspective. Given the average age of the home HD population in the United Kingdom (47–48 years old), a time horizon of 40 years is used and believed to be equivalent to a lifetime time horizon for patients with ESRD.

Methods

We constructed a Markov model to assess the cost-effectiveness of high-dose HD performed in-center or at home compared with thrice-weekly, conventional ICHD by simulating a hypothetical adult ESRD population requiring RRT. Model structure and data inputs were informed by a review of literature and renal registry reports.

Model Structure

The model comprises a number of discrete health states between which patients can move (Fig. 1) and adopts 28-day cycles to ensure consistency in calculations. Short cycles are preferable in ESRD because of their sensitivity to likely changes in health states [10,11]. From one cycle to the next, the patients may stay on their current modality, change modality, undergo a kidney transplant, or die (in any health state). To reflect clinical practice, patients may move to PD or kidney transplant during the model time horizon.

Model Inputs

Model inputs were sourced from published articles, UK Renal Registry annual reports, NHS Payment-by-Results (PbR) tariffs, and the European Renal Association-European Renal Dialysis and Transplant Association (ERA-EDTA) registry report.

Quality of Life

Patients' QOL has been shown to vary between dialysis modalities. A systematic review by Liem et al. [12] provides the main source of utilities for the model with adjustments to account for the improved QOL in patients receiving high-dose HD and for the home setting (Table 1). Culleton et al. [4] is the only randomized controlled trial to have considered the effect of dialysis dose on patient utility, demonstrating a 17.6% increase in utility from baseline in patients changing from conventional ICHD to high-dose HD at home. We assumed that half this benefit comes from the change to high-dose HD and half from the move to the home setting; consequently, in the model, patients receiving high-dose HD have utility values 8.8% higher than the utility values of those receiving conventional HD. Considering that the assumption is based on one small study, we varied the percentages of benefit in sensitivity analysis. De Wit et al. [13] reported 22.7% higher QOL values for patients on limited care HD than for patients on ICHD (0.81 vs. 0.66). The ratio of these values was applied to the utility assigned to patients on ICHD (from Liem et al. [12]) to derive the utility for patients receiving conventional home HD, assuming that the QOL of patients receiving limited care HD in the De Wit et al. study is comparable to that of conventional home HD patients.

Survival

Survival of patients receiving conventional HD in the model is estimated using survival data for European incident patients on HD published in the ERA-EDTA 2009 Annual Report [14]. Use of ERA-EDTA data requires us to assume that these patients are representative of those in the United Kingdom (in the ERA-EDTA 2009 Annual Report, UK patients represent 20% of all incident patient counts). Parametric survival models were fitted to 5-year survival data to extrapolate beyond 5 years [15]. An exponential distribution provided the best fit for HD survival data based on a comparison of Akaike information criterion values (the model with the smallest Akaike information criterion value is preferred).

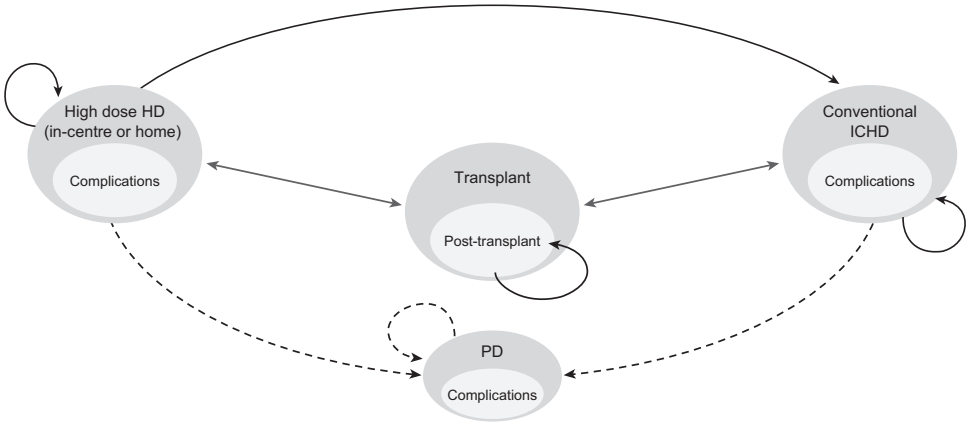

Fig. 1 – Model flow diagram. Each dialysis modality is shown as a separate health state in the model as follows: conventional in-center hemodialysis (ICHD) includes hospital or satellite; high-dose HD, in-center or at home; peritoneal dialysis (PD); transplant; posttransplant. Patients can die from any of the health states in the model. Although the emphasis of the analysis is the comparison of costs and outcomes between patients on high-dose and conventional HD, to reflect clinical practice some patients may move to PD during the model time horizon.

Table 1 – Clinical and QOL parameters and cost elements applied in the model.

Clinical and QOL parameters

Parameter	Value (range*) and parameter distribution†	Data sources
Mortality		
High-dose HD mortality HR vs. conventional HD	0.76 (0.57–0.95), lognormal	[7,8,17]
Utilities		
QOL improvement for high-dose HD	8.8% (6.6%–11.0%), beta	[4]
Conventional ICHD utility	0.56 (0.49–0.62), beta	[12]
High-dose ICHD utility	0.61, beta	[4,12]
Conventional home HD utility	0.69 (0.52–0.86), beta	[12,13]
High-dose home HD utility	0.75, beta	[4]
Transplant/posttransplant utility	0.81 (0.72–0.90), beta	[12]
Hospitalizations (%)		
Conventional ICHD hospitalization probability (28 d)		
First year	7.05 (5.29–8.81), beta	[3]
Subsequent years	4.86 (3.65–6.08), beta	[20]
High-dose ICHD hospitalization probability (28 d)		
First year	6.49 (4.87–8.11), beta	[3]
Subsequent years	4.48 (3.36–5.60), beta	[20]
Conventional home HD hospitalization probability (28 d)		
First year	5.35 (4.01–6.68), beta	[5]
Subsequent years	3.69 (2.77–4.61), beta	[20]
High-dose home HD hospitalization probability (28 d)		
First year	7.09 (5.32–8.86), beta	[5]
Subsequent years	4.89 (3.67–6.11), beta	[20]
Transplant probabilities		
Transplant rate for all modalities (28 d)	0.007 (0.005–0.009), beta	[18,22,45]
Graft failure probability for all modalities (28 d)	0.004 (0.003–0.005), beta	[18]
Transition probabilities (%)		
Proportion moving from ICHD to home HD (28 d)		
0–6 mo and 7–12 mo	0.05 (0.04–0.06), beta	Assumption
13–18 mo	0.03 (0.02–0.04), beta	
19+ mo	0	
Proportion moving from home HD to ICHD (28 d)		
Constant probability	0.38 (0.29–0.48), beta	[33]

Cost elements

Parameter	Value (range‡)	Data sources
Access costs—initial access and access maintenance due to technique failure or access failure (£)		
Vascular access cost	1,287 (965–1,609)	[21]
Dialysis services cost		
ICHD cost per session§	147	[21,46]
Home HD cost per week	456 (342–570)	[21]
ESA costs		
ESA cost per 1000 units	5.09 (3.82–6.36)	[47]
Conventional ICHD and home HD ESA dose (units/wk)	6705 (5029–8381)	[48]
High-dose ICHD ESA dose (units/wk)	5280 (3960–6600)	[3,48]
Monitoring costs (£)		
Annual monitoring cost for all patients‖	380	[21]
Hospitalization costs (£)		
Cost per (HD) hospitalization¶	1,904 (1,428– 2,380)	[21,23]
Transport cost per visit (applied only to ICHD sessions) (£)		
Weighted#	46 (34–57)	[24–26,29]
Transplant and posttransplant costs (£)		
Procedure cost**	18,579	[18,27]
Posttransplant medication cost (annual)	11,137 (8,352–13,921)	[49]

Note. The clinical and cost inputs associated with PD were included in Appendix Table 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.002).

AV, arteriovenous; ESA, erythropoiesis-stimulating agent; HD, hemodialysis; HR, hazard ratio; ICHD, in-center hemodialysis; NHS, National Health Service; PbR, Payment-by Results; PSA, probabilistic sensitivity analysis; QOL, quality of life.

* Variables were varied according to published ranges (95% confidence intervals) or by ±25% for those variables without such information.

† The distributions selected are widely believed to be appropriate choices for the model parameters and reflect best practice.

‡ For PSA, all cost inputs are assumed to follow a gamma distribution; this reflects best practice.

§ The overall ICHD cost per session is based on a weighted average of catheter access and AV fistula/graft access tariffs, £121 (£91–£151) and £152 (£114–£190), respectively. The breakdown is based on the target percentage set by the best practice tariff for 2013–2014.

‖ Patients on each modality are assumed to receive two monitoring visits a year. The cost of a monitoring visit is calculated as the average of a single professional visit cost, £132 (£99–£165), and a multiprofessional visit cost, £247 (£185–£309).

¶ A weighted average HD hospitalization cost was calculated on the basis of costs from the PbR tariff 2013–2014 and event numbers from the National Schedule of Reference Costs 2011–2012.

A weighted transport cost per ICHD visit was calculated on the basis of the following cost elements: ambulance service vehicle, £189; hospital-provided car, £27; hospital-arranged taxi, £31; hospital transport vehicle, £13; public and private transport, £5. Proportions are based on the National Kidney Care Audit, Patient Transport Survey from 2010.

** The overall transplant cost is based on a weighted average of costs of transplant from the following donors: donor after brain death, £19,804 (£14,853–£24,755); donor after cardiac death, £16,580 (£12,435–£20,725); living donor, £18,640 (£13,980–£23,300). Proportions based on data from the NHS Blood and Transplant Activity Report for 2012–2013.

Several observational studies reported differences in survival between patients treated with high-dose HD versus conventional HD [6–8,16,17]. In our base-case analysis, we assumed an overall mortality hazard ratio of 0.76 for high-dose HD versus conventional HD up to 10 years, based on the literature (Table 1) [7,8,17]. This was calculated as each study's reported mortality hazard ratio weighted by its relative treatment group size. Because of lack of long-term data, patients receiving high-dose and conventional HD are subject to equal mortality rates beyond 10 years.

Following kidney transplant, patient survival is modeled using data from the NHS Blood and Transplant Activity Report for 2012-2013 [18]. If graft failure occurs, survival is again modeled according to dialysis modality.

Dialysis Session Frequency and Duration

As recommended by the UK Renal Association [19], the model assumes that conventional ICHD comprises 3 sessions/wk. In the main analysis, high-dose HD is defined as 5 sessions/wk. Session frequency is varied in scenario analyses.

Transition Probabilities

Patients may be treated with various dialysis modalities during their time on RRT and may move from ICHD to home HD and vice versa (Table 1). To reflect clinical practice, patients may get kidney transplantation or move to PD. In the event of graft failure, patients return to their original HD setting.

Dialysis Complications: All-Cause Hospitalizations

Patients may experience complications while undergoing dialysis, resulting in hospitalization. All-cause hospitalizations in the first year are sourced from the Frequent Haemodialysis Network publications (Table 1) [3,5]. Hospitalization rates in subsequent years were estimated via a ratio of first year to subsequent year hospitalizations using data from Arora et al. [20].

Costs

Given the UK NHS payer perspective, the model uses Payment-by-Results (PbR) tariffs to approximate costs of providing RRT to patients with ESRD. In England, dialysis services are funded by the NHS as a payer on behalf of the Department of Health using the PbR system, a national tariff of fixed prices reflecting national average costs of hospital procedures with data gathered from all NHS hospitals. Tariffs for HD are based on the care setting (hospital, satellite unit, or home) and vascular access. ICHD reimbursement is on a per-session basis to account for staff costs and consumables. Home HD currently has a fixed weekly tariff intended to cover initial training and home modification costs and designed to enable the provider to recover the upfront investment over time. The home HD tariff also covers home care visits and machine maintenance costs. The model considers cost elements associated with ESRD treatment, including dialysis access establishment and maintenance [21], dialysis service [21], erythropoiesis-stimulating agents (not included in the tariff prices) [22], all-cause hospitalizations [21,23], patient monitoring [21], transportation to/from clinics [24–26], and kidney transplantation and maintenance [27] (Table 1).

Cost-Effectiveness Analysis

For base-case analyses, high-dose HD comprises 5 sessions/wk. In each analysis, the reference scenario consists of all the patients commencing conventional ICHD; alternative scenarios assume that all the patients start on high-dose HD (in-center or at home).

The current home HD tariff is set equal to three ICHD reimbursement tariffs per week [28], which provides little incentive for providers to increase the use of home dialysis, especially high-dose HD at home. To be consistent with the reimbursement mechanism for high-dose HD in-center, in addition to the existing fixed home HD tariff, we used 5 times the 2010-2011 reference costs for a home HD session (£115/session, £575/wk) as cost input to assess the cost-effectiveness of high-dose HD at home versus conventional ICHD [29].

In line with UK Treasury guidance, future costs and benefits were discounted at 3.5% per annum [30]. The main outcome measure was the incremental cost-effectiveness ratio (ICER), the cost per incremental quality-adjusted life-year (QALY).

Scenario Analysis

An additional scenario analysis was conducted in which the number of sessions per week for patients receiving high-dose HD in-center was varied to 3.5 sessions/wk (alternative nights; the minimal number of treatments per week necessary to avoid the 2-day gap in therapy [31]) because this best corresponds to regimens used in studies showing optimal outcomes [6,8,16,17]. In addition, because observational, nonrandomised data are used to calculate the survival benefit for high-dose HD versus conventional ICHD, the assumption of improved survival is tested by assuming no difference. For the in-center comparisons, the survival assumption scenario is reported for the 5 sessions/wk regimen only.

Sensitivity Analyses

One-way sensitivity analysis was conducted by replacing the base-case value of each model parameter in turn with its lowest and highest plausible values (published ranges or ±25% for variables without such information). Published confidence intervals were available for transplant graft failure rates [18] and utility values from the Liem et al. [12] study. Changes recorded in the net benefit value are presented as a tornado diagram. The net benefit value is calculated by subtracting incremental costs from the monetary value of incremental QALYs achieved based on the current UK willingness-to-pay (WTP) value. A positive net benefit value indicates that health gains exceed the incremental cost and the intervention is considered cost-effective; a negative value implies that it is not cost-effective.

Probabilistic sensitivity analysis was also performed, in which model parameters are varied according to appropriate statistical distributions reflecting best practice (Table 1). The effect of parameter uncertainty on model results can be considered by running a large number of simulations. Results are presented as a cost-effectiveness plane scatter diagram and a cost-effectiveness acceptability curve, which presents the probability that an intervention would be deemed cost-effective versus the comparator at different values of the WTP threshold.

Results

Is High-Dose HD Cost-Effective When Performed In-Center?

For the reference scenario (100% conventional ICHD), total lifetime discounted costs and QALYs per patient are £191,207 and 5.267, respectively (Table 2). High-dose HD in-center is associated with higher costs (an increase of £108,713 per patient) and more QALYs (an increase of 0.862 per patient) compared with conventional ICHD. The ICER for high-dose HD in-center versus conventional ICHD is £126,106; at the perceived NICE WTP threshold of £20,000 to £30,000 per QALY, it is not cost-effective.

The ICER for high-dose HD (3.5 sessions/wk) is £50,598, also higher than the perceived NICE WTP threshold. When high-dose HD in-center is 5 sessions/wk but no survival benefit is assumed, total costs are relatively lower, given the reduction in survival, but the overall ICER is much higher at £396,614.

Table 2 – Head-to-head comparison of conventional ICHD and high-dose HD in-center.

Comparative scenario analyses	Total costs (£)	QALYs	ICER (vs. reference scenario) (£)
Reference scenario: 100% conventional ICHD	191,207	5.267	–
100% high-dose ICHD, 5 sessions/ wk	299,920	6.129	126,106
Scenario analyses	**Total costs (£)**	**QALYs**	**ICER (vs. reference scenario)**
100% high-dose ICHD, 3.5 sessions/ wk	234,826	6.129	50,598
Reference scenario: 100% conventional ICHD, no difference in survival	191,160	5.265	–
100% high-dose ICHD, 5 sessions/wk, no difference in survival	265,802	5.453	396,614

HD, hemodialysis; ICER, incremental cost-effectiveness ratio; ICHD, in-center hemodialysis; QALY, quality-adjusted life-year.

Because sensitivity analysis demonstrated consistent results across the main comparison and scenario analyses, we present results for high-dose HD in-center (5 sessions/wk) versus conventional ICHD (3 sessions/wk). Cost and frequency of HD sessions have the greatest impact on net benefit (Fig. 2A). A higher number of HD sessions per week, or a higher tariff for those sessions, is associated with a lower net benefit. HD survival parameters were also important drivers of model results. None of the univariate parameter changes results in a positive net benefit value for high-dose HD in-center, 5 sessions/wk.

For the probabilistic sensitivity analysis, the cost-effectiveness plane (see Appendix Fig. I in Supplemental Materials found at

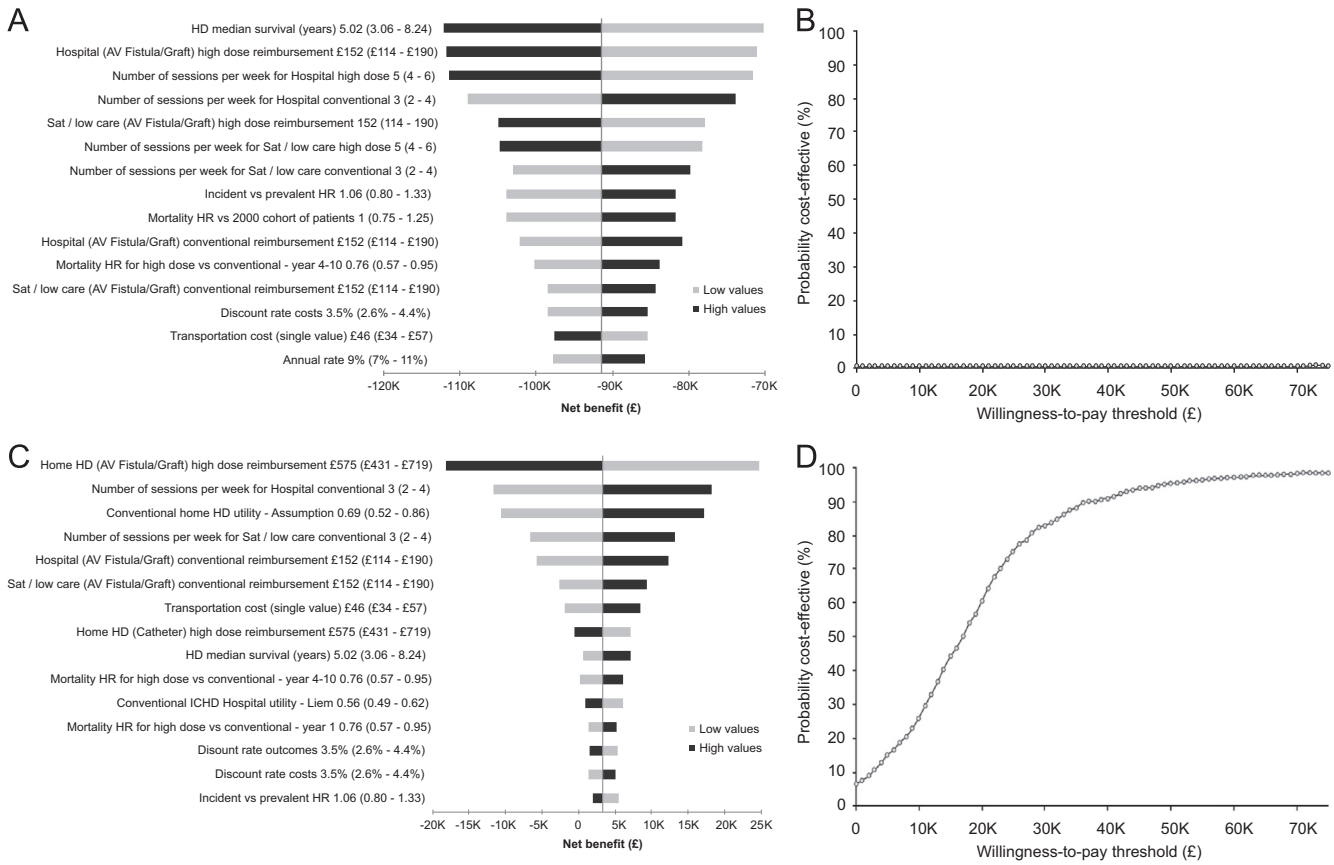

Fig. 2 – One-way and probabilistic sensitivity analyses of high-dose HD in-center (5 sessions/wk) and high-dose HD at home (increased tariff, £575/wk) vs. conventional ICHD, WTP threshold = £20,000. For high-dose HD in-center (5 sessions/wk), the tornado diagram (A) shows the sensitivity of the net benefit to changes in model parameters. Parameters that have the biggest impact on the net benefit are shown by the biggest bars at the top of the tornado diagram, whereas those that have the least impact are shown at the bottom. The cost and frequency of ICHD sessions have the greatest impact on the net benefit value. The CEAC (B) shows that the probability that high-dose HD in-center is cost-effective vs. conventional ICHD is 0% at all values of the WTP threshold (£0–£75,000). For high-dose HD at home at the increased tariff, the tornado diagram (C) shows that the biggest drivers of the results are the weekly tariff and the utility of home HD. The CEAC (D) shows that the probability that high-dose HD at home is cost-effective is 61.8% at £20,000 and 83.7% at £30,000. CEAC, cost-effectiveness acceptability curve; HD, hemodialysis; HR, hazard ratio; ICHD, in-center hemodialysis; PD, peritoneal dialysis; QALY, quality-adjusted life-year; WTP, willingness to pay.

Table 3 – Head-to-head comparison of conventional ICHD and high-dose HD at home.

Comparative scenario analyses	Total costs (£)	QALYs	ICER (vs. reference scenario) (£)
Current home HD tariff (£456/wk)			
Reference scenario: 100% conventional ICHD	191,207	5.267	–
100% high-dose HD at home	190,684	6.539	Dominant*
Reference scenario: 100% conventional ICHD, no difference in survival	191,160	5.265	–
100% high-dose HD at home, no difference in survival	171,930	5.895	Dominant*
Increased home HD tariff (£575/wk)			
Reference scenario: 100% conventional ICHD	191,256	5.267	–
100% high-dose HD at home	213,407	6.539	17,404
Reference scenario: 100% conventional ICHD, no difference in survival	191,205	5.265	–
100% high-dose HD at home, no difference in survival	192,250	5.895	1,657

HD, hemodialysis; ICER, incremental cost-effectiveness ratio; ICHD, in-center hemodialysis; QALY, quality-adjusted life-year.
* A dominant scenario is one that is associated with higher QALYs and lower costs than the reference scenario.

http://dx.doi.org/10.1016/j.jval.2014.10.002) illustrates that high-dose HD in-center falls in the upper right quadrant (i.e., more effective and more expensive) across all 1000 model simulations; the ICERs are all very high. Only ICER values on or below the £20,000 per QALY WTP threshold (indicated by the sloped line in Appendix Fig. I in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.002) would be considered cost-effective. The cost-effectiveness acceptability curve results confirm these observations (Fig. 2B): at all values of the WTP threshold up to £75,000, the probability that high-dose HD in-center is cost-effective compared with conventional ICHD is 0%, supporting the base-case result of an ICER of £126,106.

Is High-Dose HD Cost-Effective When Performed at Home?

Using the 2013-2014 PbR home HD tariff (£456/wk), we found that starting all patients on high-dose HD at home is associated with lower per-patient total costs and higher QALYs (−£522 and +£1.273, respectively) than conventional ICHD over a lifetime (Table 3). Therefore, high-dose HD at home is dominant (associated with better outcomes and lower costs).

Using a hypothetical home HD tariff (£575/wk) [29], we found that the ICER for high-dose HD at home is £17,404/QALY over a lifetime (Table 3): at the higher tariff, high- dose HD at home is cost-effective at a WTP threshold of £20,000 to £30,000 compared with conventional ICHD. Incremental costs and QALYs per patient are £22,151 and 1.273, respectively.

A scenario analysis assuming equal survival for patients receiving high-dose HD at home and conventional ICHD demonstrated lower costs and better benefits for high-dose HD at home at the current home HD tariff. At an increased home HD tariff, total costs per patient are slightly higher than the reference scenario (increase of £1045 per patient) and 0.630 incremental QALYs are accrued per patient, giving an ICER of £1657.

Sensitivity analyses for high-dose HD at home versus conventional ICHD were conducted for both home HD tariffs. The weekly tariff and the utility of home HD are the biggest drivers of results (Fig. 2C; see Appendix Fig. II in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.002).

At the current home HD tariff, the cost-effectiveness plane (see Appendix Fig. III-A in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.002) shows that high-dose HD at home falls in the lower right quadrant (more effective and less expensive) for most of the 1000 model simulations. The probability that high-dose HD at home is cost-effective at £20,000 is 97.4% and at £30,000 is 99.1% (see Appendix Fig. III-B in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.002).

At the increased home HD tariff, high-dose HD at home is associated with more QALYs than is conventional ICHD (see Appendix Fig. IV in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.002) across 1000 model simulations; however, more simulations fall above the £20,000 threshold line. With the increased tariff, the probability that high-dose HD at home is cost-effective is 61.8% at £20,000 and 83.7% at £30,000 (Fig. 2D).

Discussion

We considered the effect of treating patients with high-dose HD both in-center and at home. Differentiation was made between the settings in terms of clinical and cost outcomes. Our analyses demonstrate that high-dose HD is associated with better outcomes than is conventional HD, in terms of both life-years and QALYs.

The first base-case analysis shows that starting all patients on high-dose in-center ICHD than on conventional ICHD is associated with higher costs and QALYs. The increase in QALYs is attributed to both improved survival and QOL. Because the England ICHD tariff is paid per session, higher frequency of treatments means higher costs. The ICER for high-dose ICHD (5 sessions/wk) versus conventional ICHD (3 sessions/wk) is £126,106, much higher than the perceived NICE WTP threshold of £20,000 to £30,000 per QALY. Therefore, although the model predicts that high-dose HD in-center is more effective than conventional ICHD, costs associated with the delivery of additional HD sessions (treatment and transportation) are too high for high-dose HD in-center to be considered cost-effective.

Results for the second base-case analysis suggest that under the current PbR tariff (£456/wk), high-dose HD at home is associated with lower total costs and higher QALYs than is conventional ICHD over a lifetime; that is, high-dose HD at home is dominant. Sensitivity analysis confirmed these results. Because the introduction of the home HD tariff in 2012 has not been overly successful in increasing the uptake of home HD, it is unlikely that it will be sufficient to increase the usage of high-dose HD at home. In line with ICHD in which reimbursement is based on the number of sessions, we conducted an additional analysis increasing the home HD tariff to £575 (5 times the reference costs of one home HD session). The resulting ICER for high-dose HD at home versus ICHD was £17,404. Sensitivity analysis showed that at the £575/wk tariff, high-dose HD at home has a 62% to 84% probability of being cost-effective versus ICHD at a WTP threshold of £20,000 to £30,000 per

QALY. Threshold analysis suggests that high-dose HD at home would be considered cost-effective at a WTP threshold of £20,000 per QALY up to £592/wk and cost-effective up to £659/wk at a threshold of £30,000 per QALY.

Our finding that high-dose HD in-center was not cost-effective is consistent with a previous economic analysis that demonstrated that within a WTP threshold lower than $75,000/QALY, cost-effectiveness of high-dose HD in-center versus conventional ICHD is hard to achieve [32]. Our finding that high-dose HD at home was cost-effective is supported by a previous UK economic analysis that reported that short-daily and nocturnal home HD were associated with higher costs than was conventional ICHD, largely driven by an increase in consumables required for six sessions [9]. Both home dialysis modalities, however, were favored over ICHD because of improved patient well-being and likely cost savings from reduced transportation costs and hospitalization rates [9]. Similarly, a decision analysis examining the cost-effectiveness of nocturnal home HD (5–7 sessions/wk) versus conventional ICHD, over a lifecycle of ESRD, reported that higher frequency HD was the dominant strategy, associated with higher QALYs than in ICHD (5.79 and 5.31, respectively) and saving approximately 1.0% of total health expenses [33].

Our results may have important implications for decision makers. Substituting conventional ICHD with cost-effective high-dose HD at home meets the objectives of the current NHS Quality, Innovation, Productivity and Prevention agenda of reducing costs while improving quality of patient care [34]. Both the National Kidney Foundation and NICE's TA48 clinical guidelines, however, highlight a need to raise patient awareness of the QOL and clinical benefits associated with home HD [2,35]. Too many patients are considered unsuitable for home HD, driven by lack of patient education and strict patient selection [36]. Although it has been suggested that with appropriate education, 10% to 15% of UK dialysis patients might choose home HD as a treatment option [37], there has been no overall increase in the proportion of patients receiving home HD. In 2012, 4% of dialysis patients in England were receiving home HD [38].

The current analysis has several strengths. First, the model structure was informed by previous economic evaluations in ESRD [10,39]. Second, a thorough literature search was conducted to identify model inputs. Third, the model was validated at a clinical advisory board and with a UK-based nephrology key opinion leader who had been involved in both inpatient and outpatient NHS renal services and in NICE appraisals of HD and PD. Although the 2013-2014 PbR dialysis tariff was used for the analysis, the tariff represents the national average costs of providing dialysis care in England. In addition, consistent conclusions were drawn using PbR dialysis tariffs since 2011-2012, when a tariff for home HD was introduced.

The analyses have several limitations due to lack of high-quality data. First, the utility benefit assigned to high-dose HD versus conventional ICHD was obtained from a small randomized controlled trial but was varied in sensitivity analysis. Second, because the likely QOL decrement associated with hospitalizations was not captured, QALYs may be overestimated. Third, for some inputs such as survival, UK-specific data could not be sourced: we used data from the ERA-EDTA for baseline survival and from observational studies for survival benefits of high-dose HD versus conventional ICHD. Clinical practice in other countries may differ from that in the United Kingdom, possibly affecting the generalization of these data inputs to UK patients. We did, however, compare the patient population characteristics of patients with renal disease in the United Kingdom and Europe and conducted scenario analyses assuming equivalent survival of high-dose HD and conventional ICHD. ERA-EDTA (Europe) [40] registry data confirmed that age and sex distributions of patients in the United Kingdom are comparable to those of patients in other European countries. In addition, we tested our model with a different survival methodology, in which mortality rates from population life tables were used with adjustments made to reflect the RRT population as published by the UK Renal Registry [10,41]. This approach was not used for the base-case analysis because the relative risks published are for the total RRT population and include transplant patients. Using this approach resulted in a lower ICER (£9042) for high-dose home HD at the increased tariff. Fourth, data were not available to consider a HD dose-response relationship. Data show that the 2-day interval without dialysis is associated with increased mortality [31]; however, there is currently no conclusive evidence of the relative effectiveness of 3.5, 5, or more dialysis sessions per week. Therefore, in scenario analyses varying the number of sessions per week for high-dose HD, only costs differ between scenarios. Differences in clinical and QOL outputs are not captured. Fifth, because our analysis used PbR tariffs to approximate costs of providing RRT to patients with ESRD instead of microcosting, there may be scenarios in which tariffs do not reflect the true costs of dialysis care, especially when additional training is needed for some patients. Finally, our conclusions on the cost-effectiveness of high-dose HD at home may not be generalized to the entire UK population requiring dialysis, including those not suitable for home dialysis due to advancing age, associated comorbidities, and coping difficulties. Of those who are suitable, some may be more appropriate for PD while others may be more suited to home HD. Because of the lower costs of providing PD, the cost-effectiveness of high-dose HD at home may change significantly when compared with patients receiving PD. A targeted literature review identified that compared with patients receiving PD, patients receiving home HD are generally younger and more likely to be male [4,42–44]. Our analysis applies to situations wherein patients prefer high-dose HD at home to PD.

Sensitivity analyses in the current study confirm the base-case results, supporting home-based high-dose HD as a preferred strategy. To improve the reliability of economic evaluations, however, further contemporary research is needed to strengthen the current clinical evidence base for high-dose HD. Clinical trials remain the criterion standard for influencing changes in clinical practice. Given the nature of ESRD, with 50% 5-year survival, large-scale clinical trials to assess the efficacy of high-dose versus conventional HD, however, are unlikely [32].

In conclusion, our study shows that high-dose HD is not cost-effective when performed in-center at NICE's WTP threshold of £20,000 to £30,000 despite the model predicting that it is more effective. This analysis also demonstrated that high-dose HD at home is cost-effective versus conventional ICHD, the current standard of care for patients with ESRD. With the number of patients requiring dialysis rising annually in the United Kingdom, substituting conventional ICHD with high-dose HD at home in suitable patients could help improve patient outcomes with reasonable increases in costs.

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Supplemental Materials

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